

## REMARKS

This is in response to the Official Action of October 3, 2003. The points raised therein are addressed below in the order originally set forth.

**1.** Claims 18, 19 and 22 are rejected under 35 USC 112, first paragraph, it being indicated that applicant lists egg phospholipids as non-ionic surfactants while the prior art cited indicates that egg phospholipids are ionic surfactants, and it being alleged that a skilled artisan would be required to do undue experimentation to make and/or use a non-ionic egg phospholipid. To simplify the issues, the claims have been amended to group egg phospholipids separately from the non-ionic surfactants. Accordingly, it is respectfully submitted that this rejection may now be withdrawn.

**2.** Claims 11-18, 20, 21, and 23-28 stand rejected as obvious under 35 USC 103(a) over **Lopez-Berestein et al.** (US 2002/0143062) in view of **Chen et al.** (US 6,267,985) and **Shudo et al.** (US 5,676,146). For the reasons set forth below, this rejection is respectfully traversed.

The claims of the present invention are directed to emulsion compositions rather than liposome compositions. For example, claim 11 recites in the preamble thereof "A pharmaceutical emulsion composition...." The words "emulsion" and "composition" appearing in the body of claim 11 have been amended above to recite "emulsion composition" for the purpose of clarity and consistency, and to make abundantly clear that the instant compositions are emulsion compositions.

As noted by **Lopez-Berestein**, fenretinide is poorly soluble in water and various attempts have been made to create soluble compositions. (Column 1, paragraph 008, lines 1 - 3). As also noted by Lopez-Berestein, Gibbs, et al, (U.S. 4,665,098) described an oral composition of fenretinide that is **not** suitable for parenteral delivery. Thus, there continues to be a need for improved fenretinide compositions for parenteral delivery.

**Note also that Lopez-Berestein requires the use of tertiarybutyl alcohol in the process of making fenretinide liposomes (column 2, paragraphs 0011 and 0013), and tertiarybutyl alcohol is toxic to humans.** The present invention obviates the need for the use of tertiary butyl alcohol in the fenretinide formulation.

Lopez-Berestein only describes and teach liposomal compositions of fenretinide for parenteral administration. However, **liposomal compositions are distinct from emulsion compositions.** Liposomes are complex lipid shells that encapsulate drugs for delivery. While they can be effective in solubilizing compounds with poor aqueous solubilities, liposomes suffer from difficulty of uniform manufacture and stability, as is well documented in the general literature, and evidenced by their relatively low incidence of FDA approval. Thus, the recourse of Lopez-Berestein, et al, to liposomal formulations of fenretinide to achieve a parenteral formulation is an acknowledgement of their failure to formulate fenretinide in a more easily manufactured, and quality-controllable, composition, as provided by the distinctive emulsion formulation now claimed.

Nothing in **Chen et al.** or **Shudo et al.** teaches or provides the missing elements of **Lopez-Berestein et al.** in the context of the combination of features of the invention as claimed.

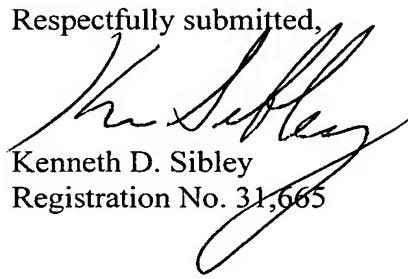
In view of the foregoing, it is respectfully submitted that claims 11-28 are nonobvious, and respectfully submitted that this rejection should now be withdrawn.

**The new claims.** The newly submitted claims are added to complete the record, and are respectfully submitted to be allowable for the same reasons as set forth above. Claim 29 employs the "consisting essentially of" transition phrase, which clearly obviates rejection based upon Lopez-Berestein which requires a different, toxic ingredient, tertiarybutyl alcohol, as noted above.

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It is respectfully submitted that this application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,

  
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